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NOTICE OF ALLOWANCE AND FEE(S) DUE

1444 7590 11/16/2009
BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

| | |
|-------------------------|--------------|
| EXAMINER | |
| WOOLWINE, SAMUEL C | |
| ART UNIT | PAPER NUMBER |
| 1637 | |
| DATE MAILED: 11/16/2009 | |

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-------------------------------------------------------------------------------|-------------|----------------------|---------------------|------------------|
| 10/593,868 | 08/26/2008 | Alex Haahr Gouliaev | FRANCH4B | 4401 |
| TITLE OF INVENTION: LIGATIONAL ENCODING USING BUILDING BLOCK OLIGONUCLEOTIDES | | | | |

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | YES | \$755 | \$300 | \$0 | \$1055 | 02/16/2010 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE
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or Fax (571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

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Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

| |
|--------------------|
| (Depositor's name) |
| (Signature) |
| (Date) |

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| 10/593,868 | 08/26/2008 | Alex Haahr Gouliaev | FRANCH4B | 4401 |

TITLE OF INVENTION: LIGATIONAL ENCODING USING BUILDING BLOCK OLIGONUCLEOTIDES

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|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | YES | \$755 | \$300 | \$0 | \$1055 | 02/16/2010 |

| EXAMINER | ART UNIT | CLASS-SUBCLASS |
|--------------------|----------|----------------|
| WOOLWINE, SAMUEL C | 1637 | 506-023000 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 _____
- 3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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| BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303 | | | WOOLWINE, SAMUEL C | |
| | | | ART UNIT | PAPER NUMBER |
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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

| | | | |
|-------------------------------|------------------------|---------------------|--|
| Notice of Allowability | Application No. | Applicant(s) | |
| | 10/593,868 | GOULIAEV ET AL. | |
| | Examiner | Art Unit | |
| | SAMUEL C. WOOLWINE | 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to papers filed 07/28/2009.
2. ☒ The allowed claim(s) is/are 1-10,12,46-48,52,53,81,82,85 and 174-181.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
 - * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No./Mail Date <u>20091105</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

/Young J Kim/
Primary Examiner, Art Unit 1637

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Iver P. Cooper on November 5, 2009. Applicant is not required to submit a summary of the interview, the substance of which was a discussion of removing limitations involving the term "preferably" and to recite these limitations in separate dependent claims.

The application has been amended as follows: Please replace claims 1, 9 and 85 with the following claims, and add claims 179-181:

Claim 1. A method for synthesising one or more bifunctional complexes each comprising a) a molecule resulting from the reaction of a plurality of chemical entities and b) an identifier polynucleotide identifying one or more or all of the chemical entities having participated in the synthesis of the molecule, said method comprising the steps of:

- i) providing a plurality of building blocks at least some of which comprise one or more chemical entities linked to an identifier oligonucleotide,
- ii) providing one or more connector oligonucleotides capable of hybridising to the identifier oligonucleotides of the building blocks provided in step i),

iii) hybridising identifier oligonucleotides of the building blocks to the one or more connector oligonucleotides,

iv) ligating identifier oligonucleotides hybridised to connector oligonucleotide(s), thereby generating an identifier polynucleotide comprising covalently linked identifier oligonucleotides at least some of which are linked to one or more chemical entities,

v) separating the identifier polynucleotide from the one or more optionally ligated connector oligonucleotide(s),

vi) reacting the chemical entities linked to the identifier polynucleotide in the absence of hybridisation between identifier oligonucleotides and connector oligonucleotides, and

vii) obtaining a bifunctional complex comprising a molecule resulting from the reaction of the chemical entities, said molecule being linked to an identifier polynucleotide identifying at least some ~~and preferably all~~ of the chemical entities having participated in the synthesis of the molecule.

Claim 9. A method for synthesising a bifunctional complex comprising a molecule resulting from the reaction of a plurality of chemical entities, wherein said molecule is linked to an identifier polynucleotide identifying one or more of the chemical entities having participated in the synthesis of the molecule, said method comprising the steps of:

i) providing a plurality of building blocks selected from the group consisting of

a) building blocks comprising an identifier oligonucleotide linked to one or more chemical entities,

b) building blocks comprising an identifier oligonucleotide linked to one or more reactive groups, and

~~c) building blocks comprising an identifier oligonucleotide comprising a spacer or hybridisation region, wherein said building blocks comprising a spacer or hybridisation region are preferably~~ connector oligonucleotides to which building blocks of groups a) and b) can hybridise,

ii) generating a hybridisation complex comprising at least n building blocks by hybridising the identifier oligonucleotide of one building block to the identifier oligonucleotide of at least one other building block, wherein n is an integer of 4 or more,

wherein at least 3 of said at least n building blocks comprise a chemical entity,

wherein no single identifier oligonucleotide is hybridised to all of the remaining identifier oligonucleotides,

wherein optionally at least one of said building blocks of group c) is immobilised to a solid support, thereby providing a handle to which an oligonucleotide of at least one building block of groups a) or b) can hybridise,

iii) covalently linking identifier oligonucleotides of building blocks comprising one or more chemical entities, thereby obtaining at least one identifier polynucleotide comprising covalently linked identifier oligonucleotides each associated with one or more chemical entities,

iv) optionally separating said identifier polynucleotide obtained in step iii) from any optionally immobilised connector oligonucleotides hybridised thereto, wherein said separation optionally comprises the step of diverting said identifier polynucleotide comprising covalently linked identifier oligonucleotides each associated with one or more chemical entities to a different reaction compartment, thereby separating said identifier polynucleotide from said optionally immobilised connector oligonucleotides,

v) reacting said at least 3 chemical entities linked to the identifier polynucleotide in the absence of hybridisation between identifier oligonucleotides and connector oligonucleotides, and

vi) obtaining a bifunctional complex comprising a molecule resulting from the reaction of a plurality of chemical entities, wherein said molecule is linked to an identifier polynucleotide identifying one or more of the chemical entities having participated in the synthesis of the molecule[[:]]

~~preferably, all chemical entities to be reacted are linked to the same identifier polynucleotide.~~

Claim 85. A method for generating a library of bifunctional complexes comprising a molecule and an identifier polynucleotide capable of identifying the chemical entities having participated in the synthesis of the molecule, or identifying the reaction steps having led to the synthesis of the molecule, said method comprising the steps of:

hybridising a plurality of building block identifier oligonucleotides to a plurality of connector oligonucleotides each capable of hybridising to one or more building block

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oligonucleotides, said building block identifier oligonucleotides being linked to one or more chemical entities,

covalently linking said building block oligonucleotides hybridised to one or more connector oligonucleotides, thereby generating a plurality of identifier polynucleotides linked to a plurality of non-reacted chemical entities,

separating the identifier polynucleotides from the optionally ligated connector oligonucleotides, ~~preferably by degrading the optionally ligated connector oligonucleotides and/or by performing a washing step wherein the identifier polynucleotides are associated with a solid support capable of being separated from non-bound, optionally ligated connector oligonucleotides~~

reacting chemical entities linked to each of a plurality of different identifier polynucleotides,

and generating a library of bifunctional complexes each comprising a different molecule and an identifier polynucleotide identifying the chemical entities having participated in the synthesis of the molecule, wherein each of the plurality of molecules are generated by reacting at least 2 chemical entities associated with different building block oligonucleotides.

179. The method of claim 1, wherein the identifier polynucleotide at step vii identifies all of the chemical entities having participated in the synthesis of the molecule.

180. The method of claim 9, wherein all chemical entities to be reacted are linked to the same identifier polynucleotide.

181. The method of claim 85, wherein separating the identifier polynucleotide from the optionally ligated connector oligonucleotides is performed by degrading the optionally ligated connector oligonucleotides and/or by performing a washing step wherein the identifier polynucleotides are associated with a solid support capable of being separated from non-bound, optionally ligated connector oligonucleotides.

The following is an examiner's statement of reasons for allowance: The closest prior art is exemplified by WO 02/074929, cited on the IDS of 05/29/2008. In the prior art method, chemical entities to be reacted are attached to oligonucleotides, which are then hybridized adjacently on a template nucleic acid to bring the chemical entities into close proximity to facilitate their reaction. There is no teaching or suggestion in the prior art of ligating, or otherwise covalently linking, the oligonucleotides and carrying out the reaction in the absence of hybridization as recited in the instant claims. The claimed methods offer an improvement over the prior art in that conditions may be used during the reaction that would not be compatible with hybridization (see page 2, lines 28-33 of specification as filed).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably

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accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL C. WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Examiner, Art Unit 1637

/Young J Kim/
Primary Examiner, Art Unit 1637